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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/964,042	09/26/2001	Ralph Weichselbaum	27373/36638A	1056

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

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09/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/964,042	WEICHSELBAUM ET AL.	
	Examiner	Art Unit	
	J. E. Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,10-13 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,10-13 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 6/9/08.

Claims 1-5, 10-13, 16 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 10-13 and 16 are finally rejected under 35 U.S.C. 103(a) as being unpatentable over Advani (1997; Int. Journ. Oncol. Rad. Biol. Phys, previously of record) in view of Carroll et al. (Ann. Surg. 1996, previously of record).

The instant claims are drawn to a method for reducing a non-central nervous system tumor mass by administering a therapeutically effective amount of an attenuated HSV to a subject having cancer wherein the HSV genome has been modified in an inverted repeat region such that the HSV has only one active gamma(1)34.5 gene, wherein the HSV is administered in an amount effective to reduce the mass of the tumor mass.

Advani (1997) is an abstract that teaches "Human U-87MG glioma cells were grown in the hind limb of athymic mice… and infected with… [HSV] R7020… the tumors were harvested… 14 days after viral injection." Furthermore, Advani teaches, "Herein we demonstrate radiation enhanced viral replication as one of the interactive effects of combining IR and attenuated HSV in treating glioma xenografts and a potential therapeutic motif in the treatment of gliomas." Therefore, Advani (1997) clearly teaches a method for treating glioma tumor growth comprising direct delivery of the attenuated HSV (HSV R7020) to the tumor.

Advani does not explicitly teach that the attenuated HSV R7020 virus could be used to treat a non-CNS tumor in vivo, nor does Advani teach the particular amount of the HSV which would be a therapeutically effective amount for reducing tumor mass.

Carroll teaches treatment of non-CNS tumor using an attenuated HSV (hrR3). Specifically, Carroll teaches a method for treating colon carcinoma liver metastasis by administering an attenuated HSV directly to cells the tumor (e.g., see abstract).

Therefore, it would he been prima facie obvious at the time of invention that the method taught by Advani would have also been able to treat a non-CNS tumor such as a colon carcinoma liver metastasis in an animal or human, with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to modify the method of Advani to treat a

non-CNS cancer because Carroll teaches that attenuated HSVs can be used to treat non-CNS-type tumors. Furthermore, the in vitro findings that taught by the Advani references are indicative of an expectation of success for directly administering the vectors to tumors in vivo. Additionally, it would have been prima facie obvious to perform routine optimization to find the amount of HSV which would be a therapeutically effective amount for reducing tumor mass. As noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Therefore, routine optimization is not considered inventive, and considering the teaching of Advani that IR treatment augments HSV replication, which would increase the HSV's antitumor activity, it would have been routine to identify the optimum amount for treating tumors. Finally, since Advani teaches that the combination of IR and HSV R7020 augments HSV replication in tumor cells, it is clear that performing the optimized method would inherently result in the a reduction of tumor mass.

Response to Arguments

Applicant's arguments filed 6/9/08 have been fully considered, but are not persuasive.

Applicants argue that (1) the Advani abstract does not expressly or inherently disclose, or suggest, the reduction of any tumor mass; (2) the Advani abstract does not disclose or suggest that administration to a patient of HSV R7020, or any other HSV modified in accordance with the claims, would be safe; and (3) the disclosures of the Advani abstract and Carroll cannot

properly be combined on the basis that each reference discloses an attenuated HSV when the mechanisms of attenuation for these HSVs are scientifically unrelated.

In response, although Advani does not explicitly teach a reduction in tumor mass, performing the method taught by Advani to treat non-CNS tumors (taught by Carroll) wherein the method is optimized for it greatest efficacy (for instance by determining the most effective doses and duration of treatment) would necessarily result in a reduction of tumor mass. This flows from the teaching of Advani that the combination of IR and HSV R7020 increases viral replication which could be an effective tumor treatment.

With respect to the Carroll reference, it is acknowledged that Carroll does not teach using an attenuate HSV encompassed by the instant claims. However, Carroll teaches that an attenuated HSV, albeit a non-claimed HSV, can treat non-CNS tumors. Furthermore, as previously indicated, Advani teaches that the claimed attenuated HSV can be used to treat CNS tumors, but is silent with respect to treating non-CNS tumors. Certainly, in view of the fact that Advani teaches that the claimed HSV would be an treatment for a specific type of tumor and in view of the teaching of Carroll that attenuated HSVs could be used to treat non-CNS tumors, there would have been at least a motivation to try using the attenuated HSV taught by Advani to treat non-CNS tumors. Furthermore, given the results of Advani (that HSV R7020 is effective for treating CNS tumors) and Carroll (that attenuated HSVs are effective for treating non-CNS tumors), there would have been a reasonable expectation that HSV R7020 would also

successfully treat non-CNS tumors. Furthermore, since Advani and Carroll are both drawn to utilizing attenuated HSV for treating tumors, it is not improper to use both teachings in an obviousness-type rejection, regardless of whether or not the mechanisms of attenuation are identical. Since Advani teaches using one attenuated HSV to treat one kind of tumor and Carroll teaches a different attenuated HSV for treating a different tumor, it would have been prima facie obvious to one of ordinary skill in the art to at least try to treat the Carroll tumors with Advani attenuated HSV.

Applicant's response also refers to the Declaration of Dr. Roizman with respect to the assertion that Advani is completely silent on the issue of tumor mass reduction.

2. The Declaration under 37 CFR 1.132 filed 6/9/08 is insufficient to overcome the rejection of claims 1-5, 10-13 and 16 under 35 U.S.C. 103 based upon the teachings of Advani (1997; Int. Journ. Oncol. Rad. Biol. Phys.) in view of Carroll et al. (Ann. Surg., 1996) as set forth because: although Advani may not expressly teach that HSV R7020 reduces tumor mass, Advani does explicitly teach that HSV R7020 can be used as an effective therapeutic for treating glioma cells. Furthermore, Carroll teaches attenuated HSVs that are effective for destroying non-CNS tumor cells. Therefore one of ordinary skill in the art would have at least been least a motivated to try using the attenuated HSV taught by Advani to treat non-CNS tumors, such as the ones taught by Carroll. Furthermore, in view of the teaching of Advani that the R7020 is an effective CNS tumor therapeutic and the teaching of Carroll that attenuated HSVs are effective non-CNS tumor therapeutics, there would have been a *reasonable* expectation that the R7020 would be an effective treatment for non-CNS tumors. Furthermore, it would be a matter of routine experimentation for one of ordinary skill in the art to optimize the method to achieve peak

effectiveness. Performing the optimized method would necessarily result in the reduction of tumor mass.

3. In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

4. Therefore, Applicants arguments are not persuasive.

Conclusion

No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner, Art Unit 1635